SPRING 2014

Quest

RESEARCH AT NORTH CAROLINA CENTRAL UNIVERSITY

Early Cancer Detection: A New Approach

SPRING 2014

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NORTH CAROLINA CENTRAL UNIVERSITY

contents

ON THE COVER
Liju Yang adds cancer cells to a plate for electrical detection at NCCU's Biomanufacturing Research Institute and Technology Enterprise (BRITE).
Photo by Ted Richardson

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OUR FOCUS ON HEALTH DISPARITIES

Dear Friends of NCCU,

At North Carolina Central University, one emphasis of our research is health disparities. In April 2013, a conference at NCCU featured leading researchers who shared their findings and exchanged ideas about causes and treatments for diseases that disproportionately affect minority racial and ethnic groups. Among the key speakers was Dr. John Ruffin, director of the National Institute on Minority Health and Health Disparities (NIMHD), who was a teacher and administrator at NCCU from 1977 until 1990.

Ruffin marveled at NCCU's changes over the past 23 years, noting in particular the establishment of the Julius L. Chambers Biomedical/Biotechnology Research Institute (BBRI) and the Biomanufacturing Research Institute and Technology Enterprise.

"You're doing fantastic work here," Ruffin said. "You can compete with anybody." But he also urged: "You need to do more. You need to expand your research portfolio. Health disparities research is not just biology and chemistry. The entire university can and should get involved."

That is excellent advice, and we are taking it to heart. BBRI researchers received a $5.7 million grant from NIMHD a year ago to examine cardiometabolic diseases that disproportionately affect African-Americans. The grant is administered by the Center for Translational Health Equality Research under the leadership of Dr. K. Sean Kimbro, director of BBRI, and Dr. Mildred A. Pointer, associate professor.

"Translational" is the key word. It describes research that applies findings from basic science to enhance human health. The projects also are interdisciplinary. For example, a diabetes outreach project in Halifax County, N.C., involves researchers and students in biosciences, nursing and public health education.

Another example is Dr. Pointer's own project, described in the current issue of Quest (page 30), which takes insights about hypertension gained in the laboratory directly to communities that can benefit from them most.

Dr. Pointer is one of four scientists profiled in this, our second issue of Quest. Each is engaged in cutting-edge research to address health disparities. We are proud to show off their work to the world.

Sincerely,

Hazell Reed
Vice Chancellor for Research
and Economic Development

Quest

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RUKAYAT USMAN,
senior pharmaceutical sciences major, is testing a neuronal cell line for response to brain derived neurotrophic factor.

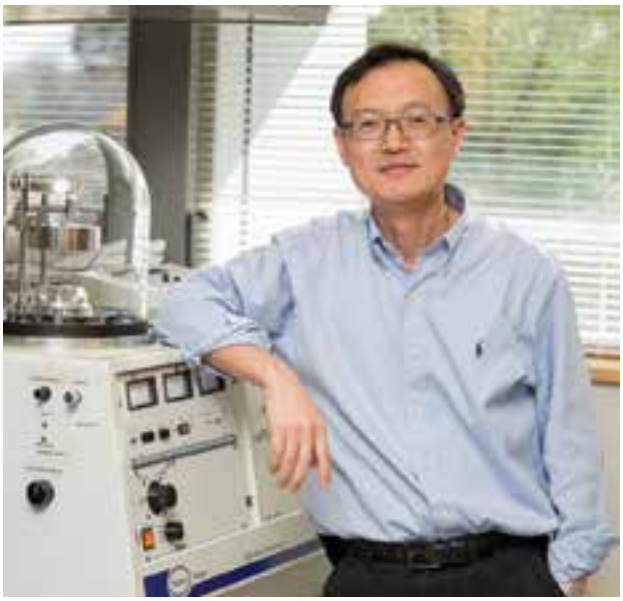
NCCU SCIENTIST AND PARTNERS RECEIVE GRANT FOR NANOSCALE 3-D PRINTER

The North Carolina Biotechnology Center has awarded $200,000 to a group of scientists and engineers from North Carolina Central University, Duke University and North Carolina State University to purchase a Dip Pen Nanolithography (DPN) unit, a device that functions as a 3-D printer at the molecular level and has a vast range of potential applications.

> "The potential of DPN applications is huge. For those with a focus on nanoscale research in biomedical, pharmaceutical and environmental fields, the DPN technique makes it possible to deliver and fabricate almost anything from pretty much all types of materials."
>
> **JOHN BANG**

John Bang, M.D., Ph.D., associate professor and interim chair of NCCU's Department of Environmental, Earth and Geospatial Sciences, who is one of the principal investigators, said the device has the ability to operate under ambient conditions — without the need for a cleanroom — and deposit features with sub-cellular resolution. "The potential of DPN applications is huge," Bang said. "For those with a focus on nanoscale research in biomedical, pharmaceutical and environmental fields, the DPN technique makes it possible to deliver and fabricate almost anything from pretty much all types of materials."

The device can deliver organic, inorganic and biological materials, including proteins, nucleic acids, lipids, hydrogels, alkanethiols, silanes, polymers and nanoparticles, in complex user-defined patterns, he said. DPN can fabricate multiplexed, customized patterns with feature sizes as small as 50 nanometers (a nanometer is one billionth of a meter) or as big as 10 micrometers (a micrometer is 1 millionth of a meter) on a variety of substrates, including glass, plastic, gold and silicon.



Bang believes groups working in a wide range of science and engineering fields — especially nanofabrication and nanomaterials; protein analysis; cell biology and microenvironment; biomolecules; cell biology and microenvironment; biomolecules, biomaterials and biointerfaces; and sensor development —

IN BRIEF

While Dr. Bang and the students he works with are accomplishing technological wonders working with materials at the nano- and micro- levels, the lab has another device that makes things that visitors can actually see and handle. The 3-D printer can be programmed to fabricate a vast range of solid objects from digital models — such as a hard plastic threaded nut and bolt (right photo).

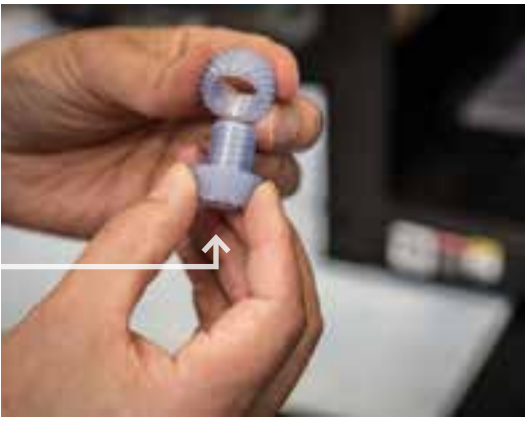
can benefit from the technology, and he welcomes their inquiries.

The device, either a unit manufactured by NanoInk of Skokie, Ill., or a comparable one, will be housed at Duke University, where it will be available for use by all the partners in the project. Delivery is expected in early 2014. Sharing in the grant with Bang are Dr. David Murdoch, Dr. Mark Walters and Dr. Gabriel Lopez at Duke and Dr. Michael Dickey and Dr. Jen Genzer at N.C. State.

Bang also recently acquired a microscale 3-D printer in his lab for both student training and scaffold generation in the field of microstereolithography, for use in a National Science Foundation-funded project to develop technological solutions to water pollution. "Both the DPN and microscale 3-D printers will be used for fabricating platforms for testing photocatalytic hybrid nanomaterials that two graduate students in my lab, Tierra Poteat and Shawn Muslim, have been building," Bang said.

By using both 3-D printers — at nano and microscales — Bang's research group eventually hopes to develop reliable deposition and delivery methods for real-life applications in the fields of environmental, biomedical and manufacturing industries, especially for the removal of chemical pollutants and biological contaminants, including microbes, from various media.

"As global markets become more competitive, helping our students engage in and have hands-on experience in the most advanced laboratory techniques will be a key to their success."



Opening Research Doors for Undergraduates

"There's something special about this. The idea is that we're going to improve the outcomes in places that need it — but we don't know everything. We need to listen and learn."

MICHAEL HAMMOND

Senior MICHAEL HAMMOND, a public health education major, is a research assistant deeply immersed in a project at the NCCU Department of Nursing, working alongside Dr. Natasha Green Leathers and Pamela Douglas. This academic year, they are heading out into the field in Halifax County in eastern North Carolina to evaluate and refine an intervention for rural African-Americans with Type 2 diabetes.

"There's something special about this," says Hammond, a paid research assistant on the project. "The idea is that we're going to improve the outcomes in places that need it — but we don't know everything. We need to listen and learn."

Hammond is one of hundreds of NCCU undergraduates in every academic department conducting substantive research under the supervision of their professors. And the university is engaged in an effort to open the doors to research for as many undergraduates as possible.

A key player in the effort is Dr. ClarLynda Williams-Devane, an assistant professor of biology who holds the additional title of undergraduate research liaison. Her goal, she says, is to create or identify research resources for all students, and she adds that NCCU is ideally positioned to do so.

"At large research universities, undergraduates often find few research opportunities," Williams-Devane says. "It can be difficult for them to get into a lab for hands-on experience. I think

continue →

"At large research universities, undergraduates often find few research opportunities. It can be difficult for them to get into a lab for hands-on experience. I think NCCU has the right combination — it's the right size, it has the facilities and a faculty that is committed to providing mentoring and encouragement." — **DR. CLARLYNDA WILLIAMS-DEVANE**

NCCU has the right combination — it's the right size, it has the facilities and a faculty that is committed to providing mentoring and encouragement."

"At NCCU," she adds, "students are often able to publish scholarly papers alongside their mentors. At most institutions, that usually doesn't happen until graduate school."

Williams-Devane, who graduated from NCCU in 2002 (B.S. in mathematics, summa cum laude), earned her Ph.D. from N.C. State University in bioinformatics, an interdisciplinary field that focuses on organizing and analyzing biological data. In the coming months, she will apply her technological expertise to development of a website that highlights what students are doing and functions as a clearinghouse.

"The website will make students and principal investigators aware of undergraduate research opportunities," she said. "We'll harness the technology to make the best use of the resources we have."

In addition to her administrative role, Willliams-Devane works directly as a research mentor with some students. One of them is Amber Esters, a senior public health education major who took a biostatistics class from Williams-Devane in 2011-12 and worked in her lab the following summer. Esters now works with Williams-Devane and postdoctoral fellow Juan Vivar at the Julius L. Chambers Biomedical/Biotechnology Research Institute (BBRI).

Amber Esters, senior public health education major

Her research involves manipulating and analyzing data on a variety of public health topics, particularly diabetes and hypertension, using a software program called RStudio — which she says is "like Excel on steroids."

"It's a great tool," Esters adds. "I learn something new every time I use it."

A continuing challenge, Williams-Devane says, is finding money and resources to support the research. "Every department has an introduction-to-research program," she says, "but in many cases, stipends or funding are not available. If a student is interested, we'll find a way to facilitate."

Dr. Hazell Reed, vice chancellor of research and economic development, is an enthusiastic supporter of the undergraduate research effort. "Our top priority is student success," Reed says, "and three-quarters of NCCU students are undergraduates. We are giving them opportunities as undergraduates to gain skills and experience that will give them an edge when they enter the work force or graduate school."

Biosciences Ph.D. Program Enters Second Year


TIMOTHY ADEKOYA


MAYANGA KAPITA


QUANTIL MELENDEZ


ANTONIO WALKER

North Carolina Central University welcomed a second class of integrated biosciences doctoral students in August 2013. The four students join the six students who enrolled in the Ph.D. program in 2012. Much like their predecessors, they have a personal commitment to tackling health disparities. Here are their stories:

▷ TIMOTHY ADEKOYA

Born in Nigeria, Adekoya came to the United States just a few years ago to continue his education, with the intention of pursuing a doctorate. He sought an atmosphere that would allow him to explore his area of interest, metabolic disorders, while also making him feel welcome. "When I came for the interview and saw the facilities and the research labs, I decided I had to come here," Adekoya said.

Doctorate students at NCCU have access to nearly 150,000 square feet of state-of-the-art science space at the Julius L. Chambers Biomedical/Biotechnology Research Institute (BBRI) and the Biomanufacturing Research Institute and Technology Enterprise (BRITE), as well as equipment and facilities on other campuses and locations.

▷ MAYANGA (CAMILLE) KAPITA

Kapita has spent a great deal of time in research labs as a student and a researcher, but he says when he came to NCCU he was impressed with the program and the faculty. He earned a bachelor's degree in physics from the University of Kinshasa in the Democratic Republic of the Congo. In 2001, Camille, as he is called, came to the United States as part of an exchange program at the University of Cincinnati. Since then he has worked in the Department of Genetics labs at the University of North Carolina at Chapel Hill.

"Working in a lab has changed my life," Kapita said. "My work is not just about scientific pursuit, but understanding the nature of diseases in order to change other people's lives."

▷ QUANTIL MELENDEZ

Melendez walked into her first doctorate classroom just five days after the birth of her daughter. A graduate of North Carolina A&T State University, she took a year off from school before beginning the doctorate program. She was originally scheduled to begin the program in 2012.

Melendez has already decided to pursue the pharmaceutical sciences track. "I am excited by the innovation of pharmacy and biology," she said. "This program lines up perfectly with my interests." Melendez spent seven years as a lead pharmacy technician at CVS and has also worked as a DNA, paternity bone marrow transplant technician at LabCorp. This program will allow her to merge her biology educational background with her retail pharmaceutical experience to develop a therapeutic drug for pediatric infectious diseases.

▷ ANTONIO WALKER

Walker is a biomedical chemical engineer who has always had an interest in health disparities research. A graduate of North Carolina State University and Virginia Commonwealth University, Walker took a leave of absence from his job at NovaTarg Therapeutics to pursue a doctorate. Making the move from engineering to pharmaceutical sciences required him to complete a year in the BRITE master's program before starting on his Ph.D.

"There are several large universities in the area, but they don't often focus on minorities," said Walker. "Having family members impacted by these diseases makes this opportunity personal for me."

A NEW APPROACH TO EARLY CANCER DETECTION

LIJU YANG'S BIOSENSORS MEASURE CHANGES IN ELECTRICAL SIGNALS TO IDENTIFY MISBEHAVING CELLS

Cancer cells, by definition, don't behave the way they should. They grow uncontrollably, spread to neighboring tissues, and then refuse to die. Most of these antics occur unnoticed until an irregular growth emerges or abnormal molecules materialize in the bloodstream. By that time, the cancer may have progressed past the point of being curable. Yet if researchers could spot cancer cells just as they start misbehaving, they might be able to nip them in the bud.

It sounds simple enough, but scientists have spent decades looking for ways to detect cancer earlier. Some efforts like the PSA test for prostate cancer have been successful, though it and others have raised enough false alarms to be deemed less than reliable. Liju Yang, Ph.D., an associate professor of pharmaceutical sciences at NCCU's Biomanufacturing Research Institute and Technology Enterprise (BRITE), may have found a promising solution.

Yang has developed a device — smaller than the palm of your hand — that can detect when cancer cells are present. Her approach merges principles of engineering, chemistry and cell biology into a technology that could not only revolutionize cancer screening, but could also help detect other situations where cells have gone awry.

Written by Marla Vacek Broadfoot | Photos by Ted Richardson

THE SECRET INGREDIENT: ELECTRICITY

Cancer only recently became a focus of Yang's research. While pursuing her doctorate at the University of Arkansas, Yang designed new devices to detect bacterial pathogens that are the major cause of foodborne disease outbreaks. Within each device Yang placed a tiny circuit board through which she could pass an electric current. She and her colleagues placed various levels of bacteria onto the electrodes, looking to see whether the presence of microorganisms like E. coli and Salmonella altered the resulting electrical signal.

Because the different pathogens behaved differently — by binding with different affinities to the molecules precoated on the electrodes — the electricity flowed through them at different rates. After a series of tweaks, her research has yielded biosensors that are able to detect distinct patterns of electrical activity for a number of different pathogens and has resulted in almost a dozen academic publications.

When Yang joined the NCCU faculty in 2006, she began to explore other applications of this technology. She had two requirements: The application should make a lasting impact on human health and it should also help her build her own research program. Cancer seemed like an obvious choice.

"Early diagnosis of cancer is crucial to successfully treating the disease and increasing the patient's chances of survival," said Yang. "Existing diagnostic methods, which rely on a combination of radiological, surgical biopsy and pathological assessment of tissue samples, are generally not sensitive enough to diagnose cancer at an early stage. I thought my technology could be used to differentiate between the electrical properties of cancer cells and normal cells for making an earlier diagnosis."

Yang sought the expertise of an associate professor in the NCCU Cancer Research Program, Xiaoxin "Luke" Chen, Ph.D., who lent Yang some cancer cells to get started. Chen studies the molecular underpinnings of oral cancer, an ideal target for Yang's technological approach.

Oral cancer is one of the most common cancers worldwide. The death rate for oral cancer is higher than that of many other frequently diagnosed cancers such as Hodgkin's lymphoma or cervical, testicular, thyroid or skin cancers, because the disease is usually not discovered until late in its development.

Left: Three-dimensional cultures of prostate cancer cells grow in stacks of plates in Liju Yang's lab at BRITE. Below: Yang, left, and undergraduate Eric McCoy at work in the lab.

Yang is hopeful that her handheld device could not only enable clinicians to diagnose oral cancer earlier but also help drug developers identify new anticancer agents that might be most successful in thwarting the disease.

But oral cancer shouldn't be so difficult to diagnose. The cells that ultimately give rise to the disease — called epithelial cells — are continuously shed into one of the body's most accessible fluids, saliva. In fact, each drop of saliva contains more than 20,000 of these cells. If some of the cells have become cancerous, they will likely turn up in the saliva, even at very early stages. Studies have shown that the number of cancer cells found in saliva actually corresponds with the stage of the disease.

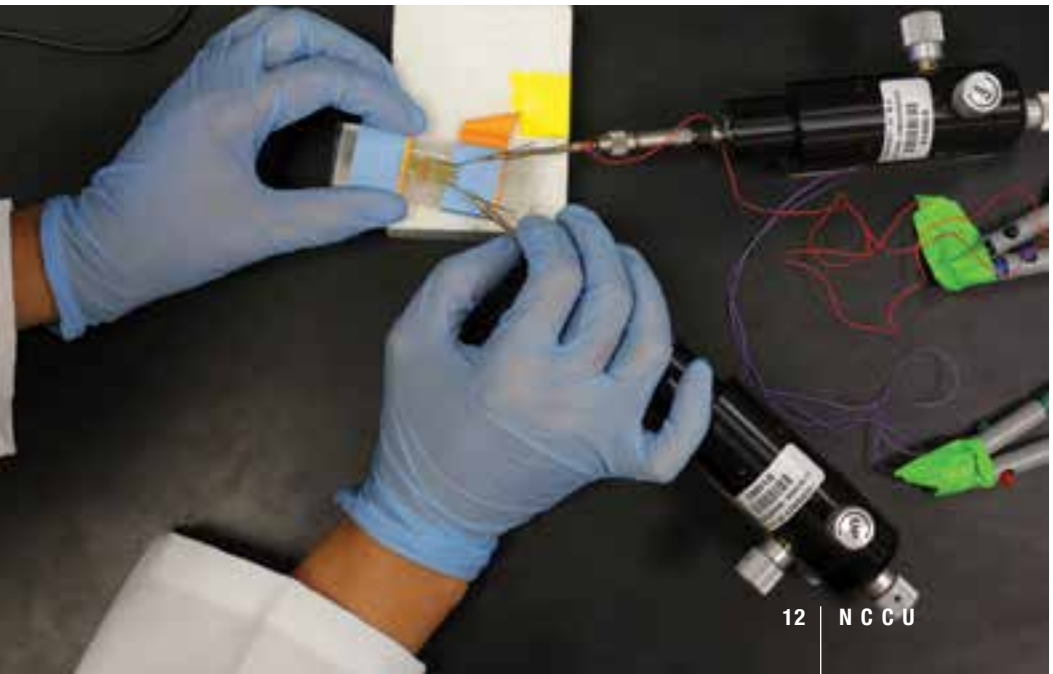
The main roadblock to diagnosis has been the lack of any clear hallmarks of early-stage oral cancer — the molecular quirks and microscopic abnormalities that geneticists or pathologists could easily recognize. Though Yang's approach could be manipulated to incorporate genetic or immunological markers of disease, in its purest form it relies on a single signal: electricity. The technique takes into account the attributes that make cancer cells unique — their uncontrolled growth, spreading and refusal to die — and translates those properties into changes in electrical signals that can be used to distinguish cancerous cells from their noncancerous counterparts.

TELLTALE MISBEHAVIORS

To test her approach, Yang ran electricity through a device containing cultured oral squamous cell carcinoma cells, which represent the most common form of oral cancer. She then measured changes in the electrical current as an indicator of the way the cells are behaving — or misbehaving — on the electrode surface. Yang repeated the experiment using normal epithelial cells and then compared these measurements — called electrical impedance — to show that there were differences between the cancerous and noncancerous cells.

She followed up that study, which was published in the journal Analytical and Bioanalytical Chemistry, by digging deeper into the specific electrical patterns associated with the miscreant properties of oral cancer cells. Yang found that the electrical impedance signal generated by the cells rose rapidly before plateauing at a specific level, akin to the exponential curves of high school math fame. The rise of the curve was affected by two characteristics — cell adhesion or stickiness, and cell spreading — which together enable cancer cells to invade neighboring tissue. The plateau of the curve was affected by the proliferation, or stacking up, of cells, which caused them to cover the electrode surface completely.

Having pinned down these telltale signs of cancer, Yang turned her attention to studying whether this technology could give insight into the effects of both anticancer drugs and carcinogens. She treated cultured oral cancer cells with the common chemotherapy drug cisplatin, placed them into the device and then measured the electrical signal. The biosensor showed that the drug did its job, knocking down the population of cancer cells and causing the electrical impedance signal to drop. Then Yang performed the same experiment, this time adding nicotine, a known oral cancer-causing agent. In a study published in the journal Biosensors and Bioeletronics, she found that nicotine interfered with cisplatin's ability to kill cancer cells.



Left: Yang connects a microchip-based sensor for cancer cell detection to an impedance analyzer.

KEEPING IT REAL

Yang is hopeful that her handheld device could not only enable clinicians to diagnose oral cancer earlier but also help drug developers identify new anticancer agents that might be most successful in thwarting the disease. But there are several steps remaining in the scientific process before that hope can become a reality. First, Yang would like to test her approach using real saliva samples, rather than the cultured cell lines that she has previously employed. Second, she is working to make her technology more predictive of the real three-dimensional world, rather than being limited by the confines of two dimensions.

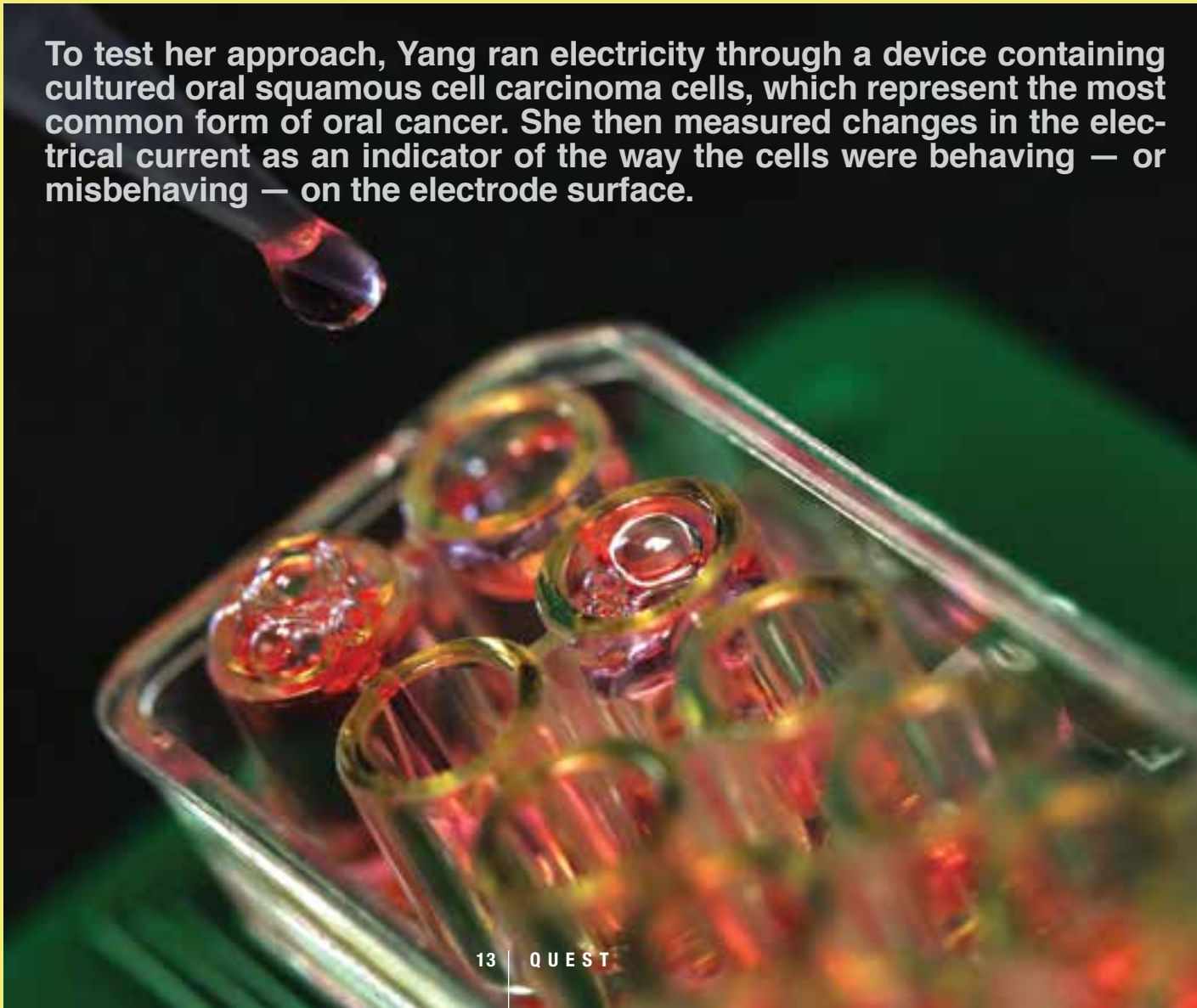
"Traditionally, when we do this type of research we grow the cells in a flask in a single layer. But the cells in our body do not lie next to each other; they are stacked together, interacting with each other in every direction," said Yang. "We think it is important to create a 3D system that more closely mimics the environment of the human body."

Members of her lab — Yang currently mentors three undergraduates and three graduate students —have already begun growing cells in 3D and are working to incorporate electrodes into a new and improved device. One of her undergraduate students, Courtney Spearman, said her time in Yang's lab has turned her on to academic research.

"I'm learning so much and getting hands-on experience at the same time," Spearman said. "I've learned how to culture cells, to do different types of protein assays, electrophoresis, western blotting, how to lyse cells — pretty much everything I need to know to conduct and analyze a drug experiment."

"In the future, I would love to see the science community reach a point at which people could be able to detect cancer at home."

RASHEENA EDMONDSON, PH.D. CANDIDATE



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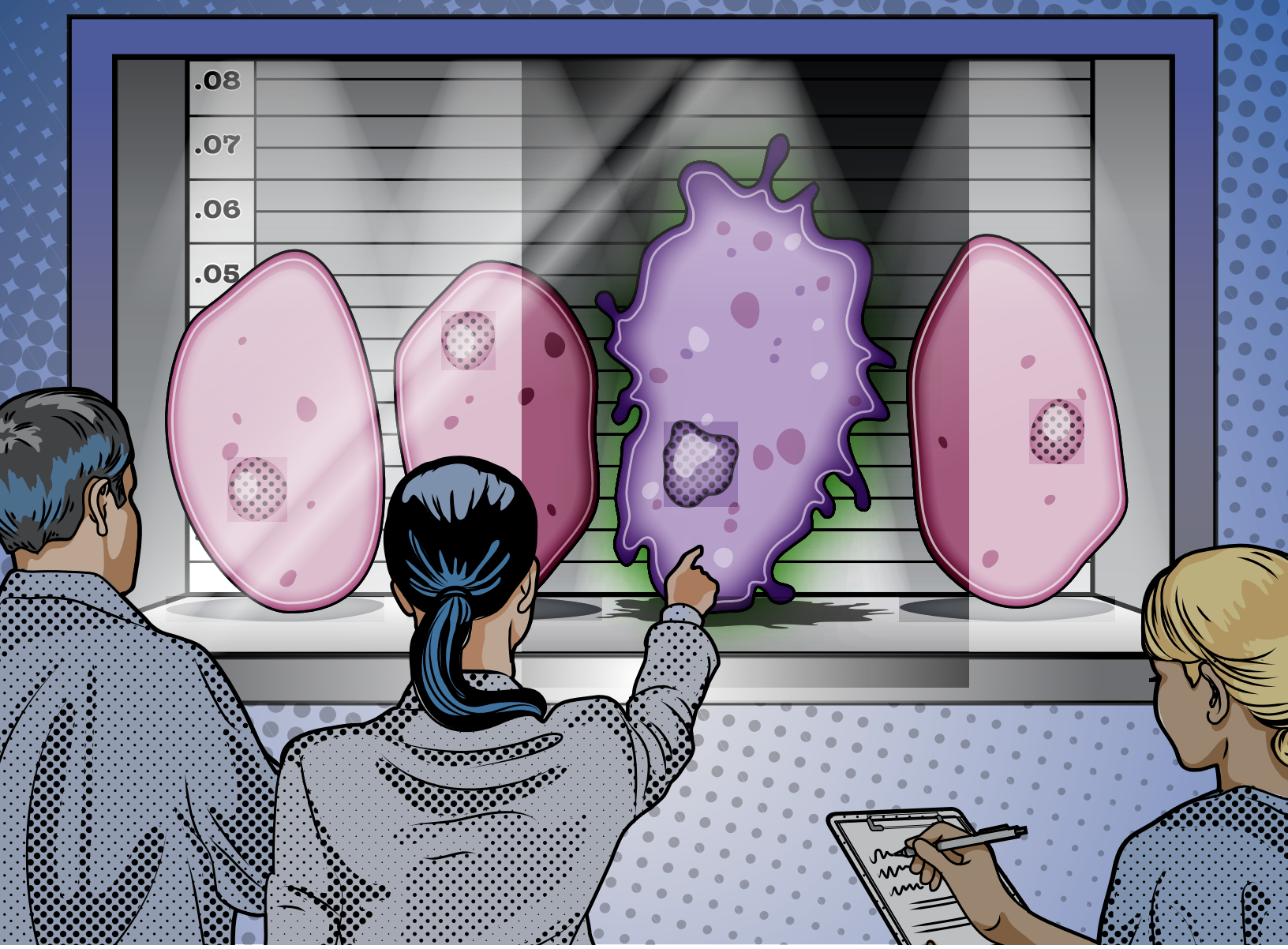


> **“Early diagnosis of cancer is crucial to successfully treating the disease and increasing the patient’s chances of survival. I thought my technology could be used to differentiate between the electrical properties of cancer cells and normal cells for making an earlier diagnosis.” — LIJU YANG**

Ph.D. candidate Rasheena Edmondson specifically joined Yang’s lab so she could work on growing tumor cells in 3D matrices. Studying how cells respond to treatment in 3D culture versus 2D is important, she said, because it bridges the gap between cell culture and in vivo. Edmondson is helping to expand the application of the technology by looking at its ability to diagnose another common disease, prostate cancer.

“In the future, I would love to see the science community reach a point at which people could be able to detect cancer at home,” Edmondson said. “Many people still don't visit the doctor regularly for a number of reasons, including not being comfortable or not having insurance. When the oral at-home HIV test came out, I was so excited. It would be wonderful if people could go into the stores and pick up tests to detect cancer like we do pregnancy tests, and of course I would love to have played a part in the development of it.”

Illustration by Tiffany DeVanzo

THE TASK master

M. RICARDO RICHARDSON'S PHILOSOPHY ON HOW TO EMPOWER MINORITY SCIENTISTS WAS SHAPED BY HIS OWN EXPERIENCE WITH A DEMANDING MENTOR

BORN IN A VILLAGE IN HAITI, Micheler Ricardo Richardson, Ph.D., might never have become an accomplished cancer researcher. Most of his childhood friends remained in his impoverished hometown of Jean-Rabel while Richardson forged his own way, traveling to the capital Port-au-Prince, then Madrid and Barcelona, before setting off to Chicago and finally Durham.

Richardson maintains that his life trajectory was driven not by determination, though he is a fan of hard work. Nor was it fueled by intellect, even though the man has plenty of brains. Rather, he says, what truly set him apart from his peers was opportunity.

"I've just been lucky," said Richardson, now a professor and director of the Cancer Research Program at NCCU. "I feel that if these guys had the same opportunity I had, they would be a lot farther today. I have always had good mentors — from my parents, to the priest in my village, to my professors in Spain or my advisors in the States. Everything I have accomplished, the credit goes all to my mentors."

Dr. Richardson with student Vandana Singh. ▷

Written by Marla Vacek Broadfoot / Photos by Ted Richardson

Above: Postdoctoral fellow Vandana Singh cultures cells in Richardson's lab at BBRI.

A LOT TO LEARN / Growing up in that tiny village in western Haiti, Richardson spent his Sundays serving as an altar boy at the Catholic church. The priest noticed a certain intellectual curiosity and focus in the young Richardson, and encouraged his parents to send him to school in the capital. At the new school, he learned about the history of penicillin and became intrigued by the potential of basic science fields like microbiology to save lives. Setting his sights on a career as an industrial microbiologist, Richardson left Haiti to study in Madrid, where his skin color lent him an air of celebrity.

"I was essentially the only black on campus. Everybody wanted to be my friend, everybody wanted to know me," Richardson recalled. "I remember my first friend in Spain would come to my class every day and take notes for me because I didn't speak Spanish at the time. She was in a completely different program, but there she was, helping me. I had so many people trying to help me in Spain, it was humbling. Originally I had planned to go from Spain to either France or Belgium, where I could speak French. But my experiences in Spain made me decide to stay."

After four years in Madrid, Richardson enrolled at the Universitat Autonoma of Barcelona, where he earned his B.S., M.S., and Ph.D. in biology. His doctoral advisor had a favorite saying at the time, "L'habit ne fait pas le moine" loosely translated as "the habit does not make the priest." In his own words, he took the quote to mean that a Ph.D. doesn't make a scientist; the degree is a "passport to travel to the scientific land." Taking his advice to heart, Richardson used his passport to gain entry to the ultimate land of opportunity, the United States.

Shortly after beginning his postdoctoral training at Northwestern University, Richardson had to return to his home country to obtain a green card. Because of

→ THE RESEARCHERS

trained in Richardson's laboratory investigate tiny chemical messengers called chemokines, which send out cellular distress signals to summon immune cells to the site of disease or injury. Chemokines have been implicated in a number of diseases where immune cells don't work the way they should, including rheumatoid arthritis, asthma and cancer.

some issues with his paperwork, he was detained in Haiti for several weeks. When he finally came back to the laboratory, he and his advisor, Marlene Hosey, had a huge argument about his commitment to research. Hosey walked out and didn't return for several days, but when she did, she handed him a freshly composed treatise several pages long called "Philosophy and Guidelines, Helpful Hints about Working in the Hosey Lab."

In it, Hosey explained why she loved her career as a scientist, outlined what she expected from members of her laboratory, and listed what it would take for her protégés to succeed in science. For instance, she stated that scientists should expect to work at least 60 to 80 hours a week to be competitive in the field.

Emboldened by youth, pride, and a bit of naiveté, Richardson hastily revised the title of her manual of laboratory wisdom to read "Philosophy of Slavery and Stupidity, Helpful Hints About Working to Dig Your Own Grave." Amazingly enough, Richardson and Hosey learned to work together again. And Richardson learned that the bits of advice Hosey had put down on paper were absolutely true.

"So much of what she wrote sounded like slavery and stupidity. But as I grew up and got my own lab, I came to realize how right she was," said Richardson, who served on the faculty at Duke University before coming to NCCU. "Believe me, you're not going to be successful in this business if you cannot put in 60 to 80 hours a week. That doesn't mean you have to spend all that time at the bench — some of it is spent reading scientific articles or writing up your results. But to succeed, you have to be willing to work hard."

Richardson has tried to instill that same work ethic in his students, who each receive a copy of Hosey's pamphlet on their first day in the lab. One former trainee, Natalie Sutton, recalls finding that introductory pamphlet to be a bit a harsh. But she later realized that it gave her the right mindset to succeed once she set foot off the NCCU campus.

"I did two other internships, one at The Ohio State and one at UNC Chapel Hill, and it seemed like a lot of people came in with this notion that research is a 9-to-5 job. That is not true at all – you have to put in the time and effort to accomplish what you set out to accomplish," she said.

Today Sutton is working as a research assistant at the N.C. State University College of Veterinary Medicine and looking into different medical school programs. She still looks back at the three years she spent in Richardson's lab as one of the best experiences of her college career.

"Knowing his story and how he came from really humble beginnings to now be known nationally and internationally for his research, it would hard to imagine someone could work with him and not end up loving research," Sutton said.

Another student of Richardson's, Kezia Addo, says she continues to turn to him for advice even three years after graduating.

"He follows up with his students," said Addo, who recently completed a post-baccalaureate program at the National Institutes of Health and is now applying for Ph.D. programs. "Even when I go to graduate school, I know that I can still come back to him and get his opinion."

THE STUDENT BECOMES THE MASTER / The researchers trained in Richardson's laboratory investigate tiny chemical messengers called chemokines, which send out cellular distress signals to summon immune cells to the site of disease or injury. Chemokines have been implicated in a number of diseases where immune cells don't work the way they should, including rheumatoid arthritis, asthma and cancer.

Richardson is most interested in how this chemokine communication gets hijacked in cancer, causing

Clearly, there is a connection between inflammation and cancer, and this connection may explain some of the disparities we see in cancer outcomes between African-Americans and Caucasians. — MICHELER RICARDO RICHARDSON, PH.D.

tumor cells to grow and spread to other parts of the body. Specifically, he has been looking at a whole host of "accessory molecules" that partner with chemokines to spur cancer development. Over the years, he has methodically teased apart a number of these complex interactions, contributing more than 60 research articles, reviews and book chapters to the field.

"Clearly, there is a connection between inflammation and cancer, and this connection may explain some of the disparities we see in cancer outcomes between African-Americans and Caucasians," Richardson said. "For example, black people may be more likely to live in less affluent neighborhoods, to breathe contaminated air, to eat unhealthy food. As a consequence, their immune systems are constantly fighting and causing inflammation. The more their bodies are subjected to inflammation, the more likely they are to develop cancer."

To develop approaches to understand and change such health disparities, Richardson is leading a joint effort between NCCU's Julius L. Chambers Biomedical/Biotechnology Research Institute (BBRI) and the Lineberger Comprehensive Cancer Center at UNC–Chapel Hill. Funded with $11.9 million from the National Cancer Institute, the PARTNERS Research and Training Program in Cancer Disparities pairs researchers from the two institutions to focus on projects related to prostate, breast, oral, esophageal, ovarian and lung cancer.

Those small teams of scientists can expand upon their own approaches to a scientific problem to generate new ideas, collaborate on a project and publish together, sharing resources like clinical samples, technical equipment, or library access that might not be available at their sister institution.

"This partnership eliminates barriers that might keep researchers at NCCU from succeeding," Richardson said. "Those resources might not exist here on campus, but our researchers now have access to them and can enjoy many of the same opportunities as researchers at UNC–CH."

For example, esophageal cancer researchers Xiaoxin "Luke" Chen, Ph.D., a professor at NCCU, and Nicholas Shaheen, M.D., MPH, a professor of medicine at UNC–CH, came together to look for genetic and environmental factors that may contribute to the racial disparity seen in a precancerous condition called Barrett's esophagus. Shaheen provides clinical expertise and tissue samples from patients with the disease, while Chen provides the laboratory expertise and molecular analysis. Their collaboration has been one of the most fruitful of the program, generating a dozen publications to date.

Despite all that he has accomplished as leader of the PARTNERS Program, director of the Cancer Research Program, and principal investigator of his own laboratory, Richardson wants to do more than pursuing scientific knowledge. He says he won't feel that he has completed his life's work until he has returned to Haiti to mentor and teach the youth in his old village.

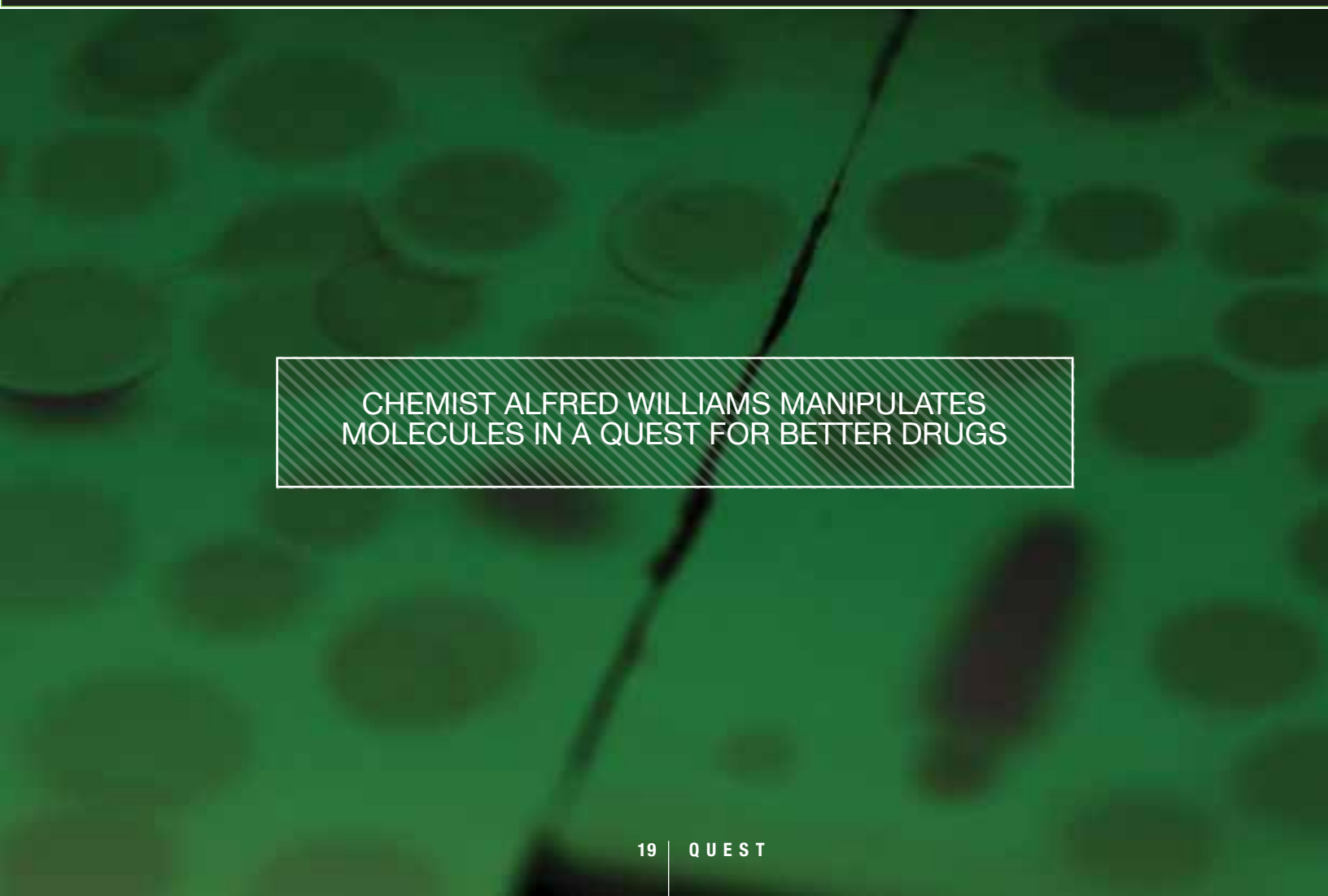
"What can you call an accomplishment when you come from a country where 20 percent of children still die before the age of five? I don't think anything I've done scientifically means much when you compare it to the dire circumstances children face there every day," Richardson said. "I want to help the people who helped me in my village and show them what is possible."

One day Richardson plans to retire and become the principal of his old school. But for now, he is content to pursue his scientific interests and continue to shape young minds closer to home, giving them some of the same opportunities that made such a difference in his own life.

TWEAKING WHAT NATURE PROVIDES

IN THE EARLY DAYS OF DRUG DISCOVERY, our ancestors made medicines from what they found in the woods, chewing herbs to ease stomachaches or wrapping leaves around wounds to help them heal. But today, rather than forage through the forest looking for cures, chemists can take the natural products their ancestors procured and build them from scratch in the laboratory, where they might tweak the chemical structures to make better drugs.

Written by Marla Vacek Broadfoot / Photos by Ted Richardson



CHEMIST ALFRED WILLIAMS MANIPULATES MOLECULES IN A QUEST FOR BETTER DRUGS

ALFRED WILLIAMS, PH.D., is one such synthetic and medicinal chemist. His laboratory at NCCU's Biomanufacturing Research Institute and Technology Enterprise (BRITE) is like a miniature drug company, where he can tinker with medicinal products found in nature, as well as with compounds created by pharmaceutical giants like Merck or uncovered through the efforts of his collaborators at BRITE, who screen small molecules for drug candidates.

"Natural products are a good starting point for drugs because many of them have beneficial properties that could be effective against ailments like cancer, infection or neurodegenerative diseases," explained Williams, an associate professor of pharmaceutical sciences. "The problem is that what we find in nature usually isn't in the right form to make a drug. My job is to develop the chemistry for making those compounds, at the same time looking at ways to engineer new structures that will make the drugs more potent and effective."

AN UNLIKELY LOVE

Williams' work is firmly rooted in a love for organic chemistry, a subject that even some of the most ardent science lovers are eager to put behind them. While those complicated chemical structures and reactions have proved to be challenging for many, to Williams they provided the building blocks for something new and meaningful.

"I like building things," Williams said. "That's what gets me excited — when you create something that nobody has made before, or when you invent a new approach to making drugs that nobody has tried before."

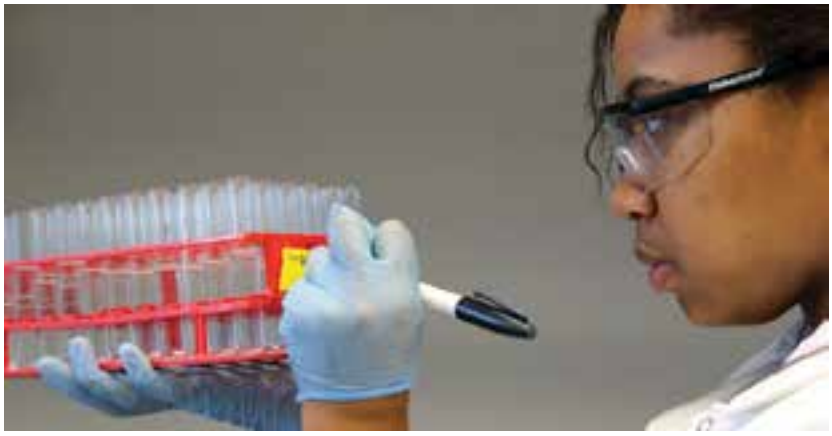
While still an undergraduate, he began to explore new ways of creating chemical compounds and putting structures together in different configurations to see what would happen. After finishing his bachelor's degree in chemistry, Williams stayed on at San Diego State University to pursue a master's in organic chemistry before moving to N.C. State University to earn his Ph.D. in the field.

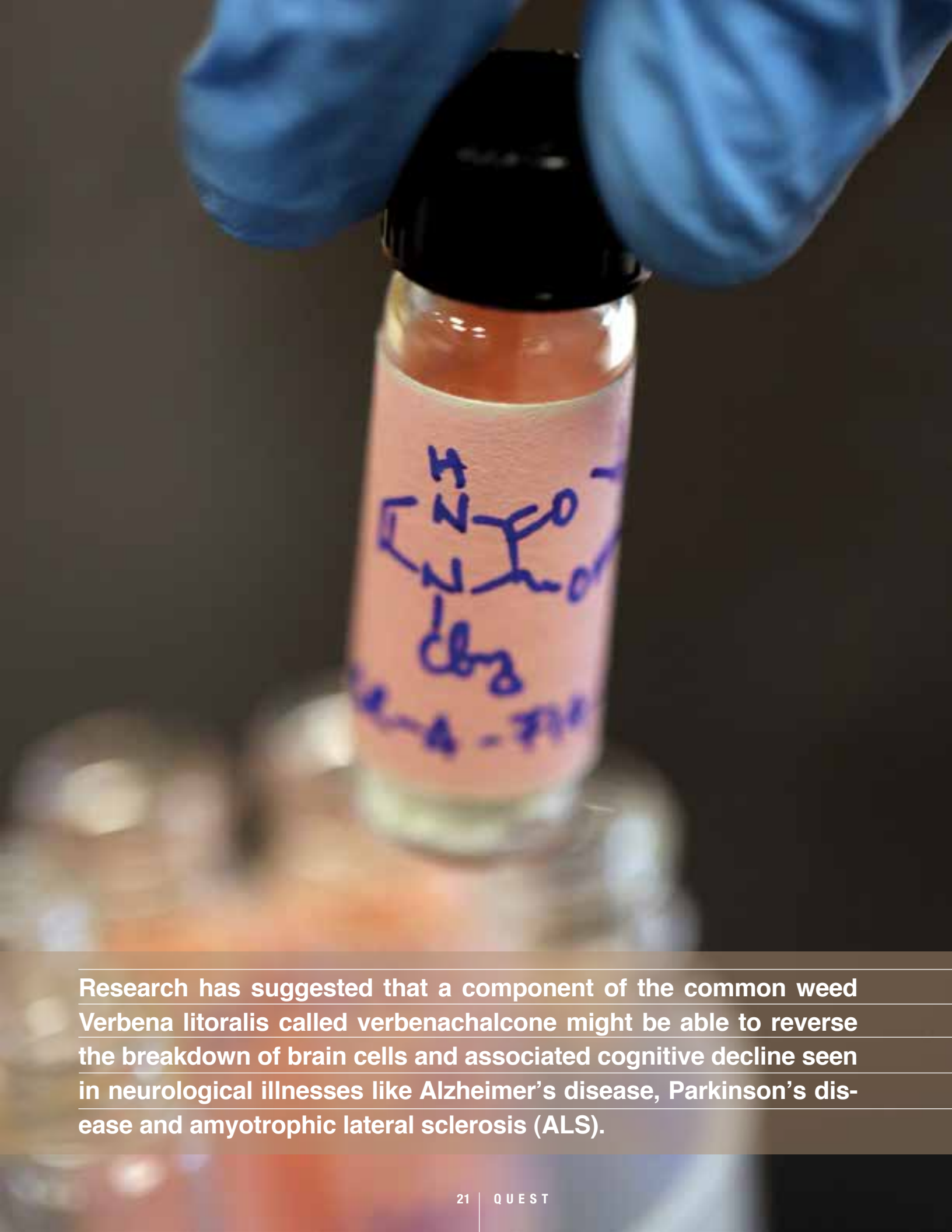
Williams then spent 10 years in industry at Eli Lilly & Co. as a senior research scientist and at R.W. Johnson Pharmaceutical Research Institute as an associate scientist. During that time, he took a hiatus from the natural products arena, instead working to synthesize a number of proprietary compounds to optimize their drug-like properties. When the opportunity arose to join the faculty at NCCU, he jumped at the chance to flex his creative muscles and share his passion for organic and medicinal chemistry with budding scientists.

"In industry you have to work on whatever is in the pipeline, but in academia you have more freedom to explore and be more creative," Williams said. "To be successful in natural products synthesis, that creativity is absolutely essential."

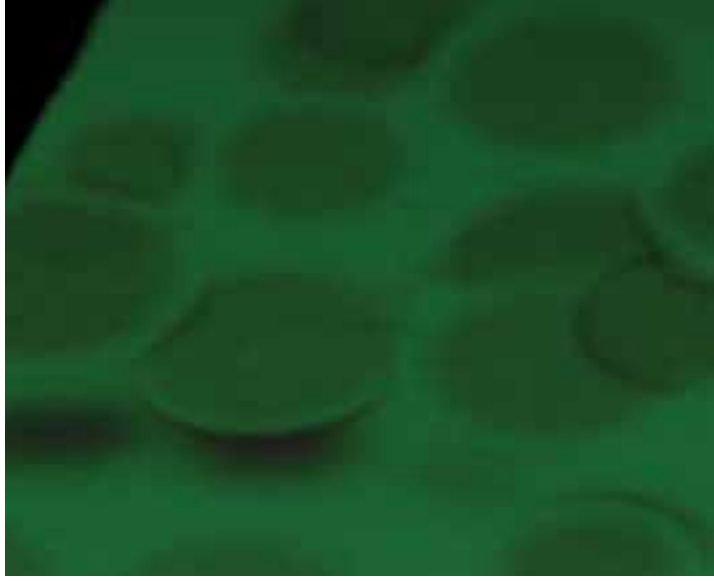
Over half of the drugs now available, such as the antibiotic penicillin and the chemotherapy drug Taxol, were derived from

Undergraduate student is Chanel Wilson labeling a rack of test tubes containing a compound that she purified using silica gel flash chromatography.





Research has suggested that a component of the common weed Verbena litoralis called verbenachalcone might be able to reverse the breakdown of brain cells and associated cognitive decline seen in neurological illnesses like Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (ALS).



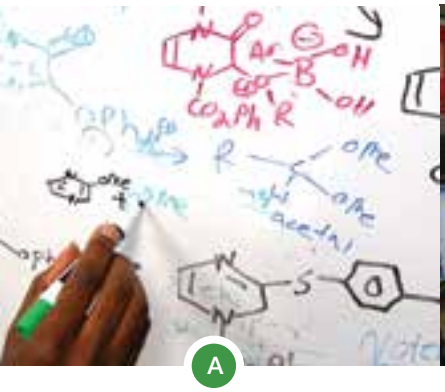
natural products. But in the 1990s the pharmaceutical industry turned its focus away from natural products in favor of a method known as combinatorial chemistry to cut and paste together millions of combinations of chemical structures in the hopes of generating useful new drugs. That approach hasn't been very successful, so many organic chemists are now going back to the natural world for inspiration for new therapeutic candidates.

For example, research has suggested that a component of the common weed Verbena litoralis called verbenachalcone might be able to reverse the breakdown of brain cells and associated cognitive decline seen in neurological illnesses like Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (ALS). Williams and a research scientist in his group, Srinivasa Dandepally, Ph.D., teamed up with their NCCU colleague Gordon Ibeanu, Ph.D., to make synthetic versions of this substance and test whether they could protect against the effects of these devastating diseases.

Before he could synthesize it, Williams first had to break the natural substance into its basic chemical structures, much as a child would pull apart a Tinkertoy set. Then he redesigned the molecule from scratch in the lab, deciding piece by piece which parts or chemical side groups would make the most effective drug.

"We look at the molecule and see what side groups would be affected if it were taken as a drug," Williams said. "Then we just choose particular groups that can hopefully minimize the metabolism or maybe enhance the potency, based on the knowledge that we have."

Thus far, Williams and Ibeanu have generated and tested several molecules that may help neurons regenerate so the brain can repair the damage wrought by disease. So far, their studies have been confined to neurons grown in the laboratory, but they hope their most promising compounds will be tested in animal models, and one day in humans, as a new treatment for neurodegenerative diseases.



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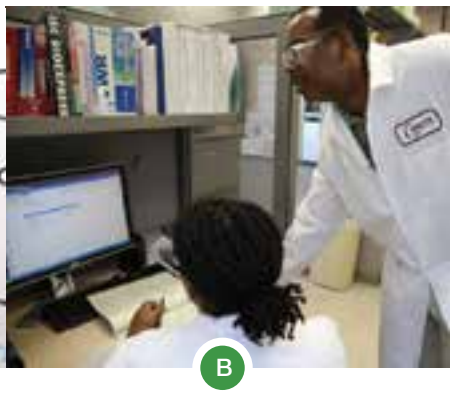

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(A) Dr. Williams instructs instructing undergraduate student Sabree Burbage on using the chemical drawing software Symyx Draw.

(B) Silica gel TLC plates are used for detecting UV active small molecules during their purification.

A NEW SET OF TOYS

Williams admits that breakthroughs can come to him at inopportune times, while on vacation or at night, when his dreams are filled with chemistry's esoteric renderings of letters, arrows and chemical structures.

"I am constantly thinking and wondering if there is a better way to approach a problem," Williams said. "Literally, I have had to get up in the middle of the night and write down an idea, because if I don't it will be gone. It could be something that could get you over a hurdle that has stood in your way."

His dreams have paid off, inspiring Williams to apply his organic chemistry know-how to create better neuroprotective therapies, anti-tumor agents and antifungal antibiotics. He is particularly enthusiastic about an NIH-funded foray into the world of anti-parasitic drugs. Specifically, Williams is working on an old Merck drug called praziquantel (PZQ), which is used to fight a disease known as schistosomiasis or "snail fever." Among human parasitic diseases, schistosomiasis ranks second behind malaria in terms of social, economic and public health importance, infecting approximately 200 million people worldwide.

Because PZQ is the main drug used to treat this endemic disease, many clinicians have worried that parasites will eventually become resistant to the drug. One solution would be to develop alternate versions of the drug that could be used if any superbugs emerge. However, the two current processes for making PZQ aren't amenable to such chemical tweaks. Recently, Williams dreamed up a third way to make the drug, working off of an organic compound called pyrazine that is often used to derive food additives. After

We look at the molecule and see what side groups would be affected if it were taken as a drug. Then we just choose particular groups that can hopefully minimize the metabolism or maybe enhance the potency, based on the knowledge that we have."

—ALFRED WILLIAMS

smoothing out a few kinks, Williams, Dandepally, and senior scientist Valentine St. Hilaire, Ph.D., found that they could use this new process to produce large quantities in the laboratory.

Undergraduate student Chanel Wilson has been helping Williams generate different versions of PZQ, which collaborator Conor Caffrey, Ph.D., at the University of California, San Francisco, is testing on the tapeworms that cause the disease.

Though any new potential drugs to come from their studies will need to move through the pharmaceutical sector before they can become reality, Williams has no plans to follow his newly discovered compounds back to industry. He joined academia, he said, so he could expose young minds to the joys of medicinal and organic chemistry, and his laboratory has given a number of students interested in the sciences, drug discovery, or even pharmacy school hands-on experience in the discipline.

Wilson, who has set her sights on pharmacy school, has enjoyed the trial and error, behind-the-scenes look she has gained into the development of new compounds and new ways of synthesizing drugs. "Now I can apply what I have learned and I can explain to a patient what is in a medication or why it might have this effect on people," she said. "I thought that would be cool being able to have a hands-on experience with this medication."

Even if all his students don't end up with that love of medicinal chemistry, Williams hopes they will at least understand its purpose.

"I get a lot of 'aha!' moments in my laboratory," he said. "The students might be sitting in their organic chemistry class, studying chemical reactions, but they don't really get it until they come and apply that knowledge in the laboratory. I'm trying to connect the dots so they can actually see how drugs are made from the beginning to the end, and that there's a reason we do what we do."

Illustration
by Tiffany DeVanzo

PERCEPTION vs. REALITY

HISTORIAN JOSHUA NADEL'S BOOK CHALLENGES LATIN AMERICA'S SOCCER MYTHS

JOSHUA NADEL, PH.D., is an assistant professor of Latin American and Caribbean history and associate director of the Global Studies Program at NCCU. His book, "Fútbol!: Why Soccer Matters in Latin America," is scheduled for publication by the University of Florida Press in early 2014, in advance of the World Cup competition in Brazil.

Nadel received his doctorate from UNC–Chapel Hill in 2007. He discusses his book and his research about soccer with Rob Waters, a writer and editor in the NCCU Office of Public Relations.

Q. A central theme of your book is that soccer "can act as a window into both the dominant and hidden histories of Latin America." This seemed to come through most clearly when you were dealing with questions of race. Tell us a bit about what you found.

Let's start with Brazil. People in Brazil and all over the world perceive that there's a particular style of soccer the Brazilians play — that it's "the beautiful game," *fútebol arte* in Portugese — and that the style is innate. It is supposed to be free-flowing, improvisational and offense-minded. What I say in the book is that these are completely constructed narratives, and that there's nothing innate about style. It's practiced, something you develop over time.

But what I found troubling and interesting about Brazil is that the style is based on late 19th-early 20th century conceptions of race. And they go back even further to theories of racism in the 1850s that attached certain traits to every race. The innate traits associated with people of African descent were improvisation, lack of rationality, an inability to plan, a passion, whereas the traits associated with Europeans were rationality and intellect. And the people who conceived of *fútebol arte* basically drew on those.

For me, it was about cracking this myth — the idea of an innate Brazilian style, this free-flowing game — to show it as this construction that's based on really racist, racialist notions of what it meant to be black and white. The concept started to take shape in the 1930s. By the time the team won the World Cup in 1958 and again in 1962, led by Pelé and Garrincha, two amazing players, they seemed to turn the myth into reality. They were this mixed-race team.

Q. Don't most Brazilians think of their country as a mixed-race society?

Definitely, but the perceived style was a construction of intellectuals who had what amounted to a very conservative view of race. It seemed radical at the time, when Gilberto Freyre, one of Brazil's most prominent intellectuals, said, "We are a racial democracy, we are a mixed-race country." People looked at him very askance. But that myth that Brazil is not rational, that it plays this open free-flow game based solely on skill and innate talent, and not at all on training or coaching, has spread across the world. The idea that they win because they're Brazilian — I think there still some belief in that.

The whole idea does an injustice, or at least a disservice, to the Brazilian soccer establishment, which was among the first to embrace the science of sport. The 1958 team that everyone looks at as the culmination of improvisation and innate skill and raw talent was in reality the most advanced of its time in terms of physiological science and sports psychology. The Brazilian federation sent scouts not only to the teams they knew they were going to play but to teams they might play. They sent scouts out to all the European championships and qualifying matches.

PERCEPTION vs. REALITY

Lee Dos Santos/ModernWorldPhotography.com

Q. That sounds very rational.

They were totally prepared. They went to Sweden, the host country, and reserved their hotel a year before. The hotel was in a place they thought they'd be able to train a little bit away from the media circus. And they asked the hotel, at least temporarily, to let go of all the female staff — something that would never happen today — because they didn't want any distractions. (Never mind that Garrincha did in fact father a child while he was in Sweden). They had a team psychologist and a team dentist. They had a team dietician. They were way ahead of what other teams were doing in terms of preparation.

So the idea that fútebol arte is all about innate talent and African irrationality and improvisation does a disservice to the institutional organization of Brazilian soccer, leaving aside what it says about ideas about race.

Q. Your chapter on Honduras also has some interesting racial angles.

Honduras is a different case in some ways, and in others it's similar to Brazil. Brazil may have been using old-school racialist ideas, but at least they were accepting that Brazil is a mixed-race nation. Honduras, meanwhile, is erasing its African heritage.

In the dominant narrative of Honduras, it is a mestizo nation, meaning a blend of indigenous and European. And according to that narrative, only a small percentage of the population — about 2 or 3 percent — is of African descent. But when you look out over the soccer field, the national team is at least 50 percent Afro-Honduran. That struck me as an interesting way to enter into the question of racial identity in Honduras and the construction of race there, and to look at how in the early 20th century, through the use of censuses and other policies, Afro-Hondurans were basically written out of history.

Starting in the 1920s and '30s, the government engaged in a concerted effort to minimize the African descent in Honduras. Again, this was based on the ideas of scientific racism that suggest that the only way you're going to advance is to become whiter, because there are innate traits tied to races. And rationality was seen as the sole province of Europeans.

Before then, Hondurans had a range of choices for racial identity. They could be "European"; or mestizo, meaning European and indigenous; or mulatto, which in this context meant European and African; or ladino, a general term that simply means mixed race. But then ladino was removed from the census altogether and replaced by mestizo. So a term for mixed race that included Africans was replaced by a term that excluded them, and it wasn't restored until after 2000. There was no place in the census for people of African descent.

As in the United States, if you're not classified in the census, then it's impossible to study what's going on in a community or figure out how to create policies to help that community if it has particular needs.

So historically, blackness was written out of Honduras. But looking at soccer allows you to question that dominant narrative. It opens up a different window.

Q. The contrast between the mestizo myth and the reality that existed on the soccer field was huge. What's the level of awareness of this disparity in Honduras today? Has the reality altered the dominant narrative?

That's hard to say. The reality of race in Honduras today is different, and I suggest that part of that is due to soccer. The players on the national soccer team have become much more vocal in the last five to 10 years, speaking out about the racism they encounter. This has coincided with a much greater activism on the part of Afro-Hondurans. Since the late '80s and early '90s there has been intellectual interest in uncovering African roots in Honduras. But soccer players get some credit for bringing it to the fore.

You still have people coming out in the press as late as 2002 or so saying that people of African descent are a detriment to the team. That debate is playing out. But the team has been playing exceptionally well in the last few years. They made it to the semifinals of the Olympics, and made it pretty far in the World Cup as well.

Q. You focus a lot on the perceived soccer styles. Argentina has *la nuestra*, Brazil has *fútebol arte*, Uruguay has *garra charrua*, and so on. These styles have a dominant narrative of their own — the idea that something about each nation is reflected in the style of soccer its best players exhibit. How much is real and how much is myth?

"The U.S. and Northern Europe — Scandinavia, France, England and Germany — are much further ahead in terms of supporting women's soccer on a national level on a regular basis. In Latin America, there's still a good deal of pushback against women playing soccer, because people still fear that it calls their sexuality and femininity into question."

— JOSHUA NADEL

There are, in fact, different preferred styles in different countries. But those are preferred styles, not innate styles. To take Uruguay's *garra charrua*, for example. It translates as Charruan tenacity, named for an indigenous tribe that was pretty much wiped out by the Spanish. It's a willingness to fight against all odds, as exemplified by the indigenous people in their fight against the Spanish.

For Uruguay to claim this as its style, as a rallying point, makes sense. It's a tiny nation surrounded by Brazil and Argentina, both of which have tried to control it, annex it and mess with its independence. So it makes sense for them to say, "We're small, we're fighting this much bigger force, and we will fight to the death to defend ourselves."

I think coaches instill in the players an element of this never-say-die attitude, and that does rub off in the play. For a long time Uruguay was focused much more on defending itself by any means necessary. They were viewed as a rough, occasionally cheap team. You could argue that the most recent embodiment of that is Luis Suarez, this phenomenal striker who plays for Liverpool in England but who is also involved in all sorts of scandals. Recently, he bit another player in a match and was suspended for 10 games.

But Uruguay punches above its weight in soccer, and always has. It won the World Cup in 1930 and 1950 and the Olympics in 1924 and 1928, which were then also considered world championships. There's no reason why Uruguay should have won any international championships, except they have had some phenomenal players.

In Argentina, there's this national mythology of the poor boy who skips school to play on a vacant lot where the ground isn't really level, and you have to learn how to control the ball through all these bumps and potholes, and this is what gives birth to this style of play that's fast and very individually oriented. It's contrasted with the team play and the supposed rationality of the Europeans. The myth, from the Argentine or Brazilian narrative, is that there's no skill in European play — that it's all practice. They're just robots on the field. They don't have any creativity at all.

The same with Brazil. Brazil has won the World Cup playing open, free-flow soccer, but it won the World Cup in 1994 playing a very contained, defense-oriented game, scoring very few goals. I don't think there are many people in Brazil who would trade winning the World Cup for losing and playing with style, but the Brazilian teams from the '80s are probably seen as much more beloved than the 1994 team, because those teams were seen as quintessentially Brazilian, free-flowing with all these crazy characters.

Q. Your final chapter is about women's soccer. Latin America seems to lag well behind the United States and Europe in its attitude toward female athletes.

I found this chapter to be the most intellectually interesting in the book, perhaps because I'm a feminist. And the way women's soccer is dealt with in the world is still pretty infuriating.

In some respects, the United States isn't so far ahead of Latin America. In the

way the team is marketed and treated, I think you still see a distressing amount of sexism. Every article you read about Hope Solo talks about how pretty she is before it talks about the fact that she's an amazing goalkeeper. You talk about Brandi Chastain in the 1999 World Cup, people still mostly think of her ripping off her shirt. There are still women's soccer players who are posing for men's magazines.

So there's still this idea that you need to show that you're feminine in order to play. To get support for the team, you have to show that the team is feminine. These attitudes still exist in the United States, and I think they exist everywhere. The French national team has done a naked calendar. FIFA, the international soccer federation, has articles about the women's sport where they talk about the players' fashion choices instead of their athleticism. You would never see a comparable article about men.

Q. If it draws fans and sponsors, what's the harm?

Numerous studies show that these attitudes are detrimental to taking women's sports seriously. When you market a sport based on femininity, what you do is diminish the athletic accomplishments of the women.

The U.S. and Northern Europe — Scandinavia, France, England and Germany — are much further ahead in terms of supporting women's soccer on a national level on a regular basis. In Latin America, there's still a good deal of pushback against women playing soccer, because people still fear that it calls their sexuality and femininity into question. It is still perceived as being a risk to their fertility. All of these sentiments are still present in Latin America.

Q. There's always been the macho stereotype about Latin America. Is that a factor?

I'm not a big believer in the whole idea of Latin American machismo. Maybe the sexism and paternalism and patriarchalism are more explicit in Latin American society than in our own, but it's there in our society too. So for us to just say, "Oh it's a macho thing," reflects an incomplete understanding of Latin American society.

There is, however, a sense in Latin America that women cannot or should not play soccer — although in the first part of the 20th century women's soccer leagues did get some level of support. They weren't attracting fans the way the men's teams were, but you did have vibrant recreational leagues in Brazil in the '30s, in Costa Rica in the '50s. And there were leagues and teams playing in the 1910s in Chile.

Q. What changed?

My sense is that they were generally left alone for a while. But in the '20s, England banned women's soccer. There had been vibrant women's soccer there in the 1910s and before, but after World War I, the football association and the Lancet, which then as now was one of the most respected public health journals in the world, published an article that said women should not play soccer, because it's too rough and it will damage their reproductive organs. So England banned women's soccer by telling all of the men's teams that if they allow women to play on their fields, they'll be kicked out of the league.

That was when questions about women's soccer started to come into play. The ban didn't happen in Brazil for about another 20 years — you really need a kind of interventionist government to actually get involved at that level, and that was the case in Brazil in the 1940s, when President Getúlio Vargas started trying to get the state involved in every aspect of people's lives.

Q. But you say very little has been written about women's soccer in Latin America?

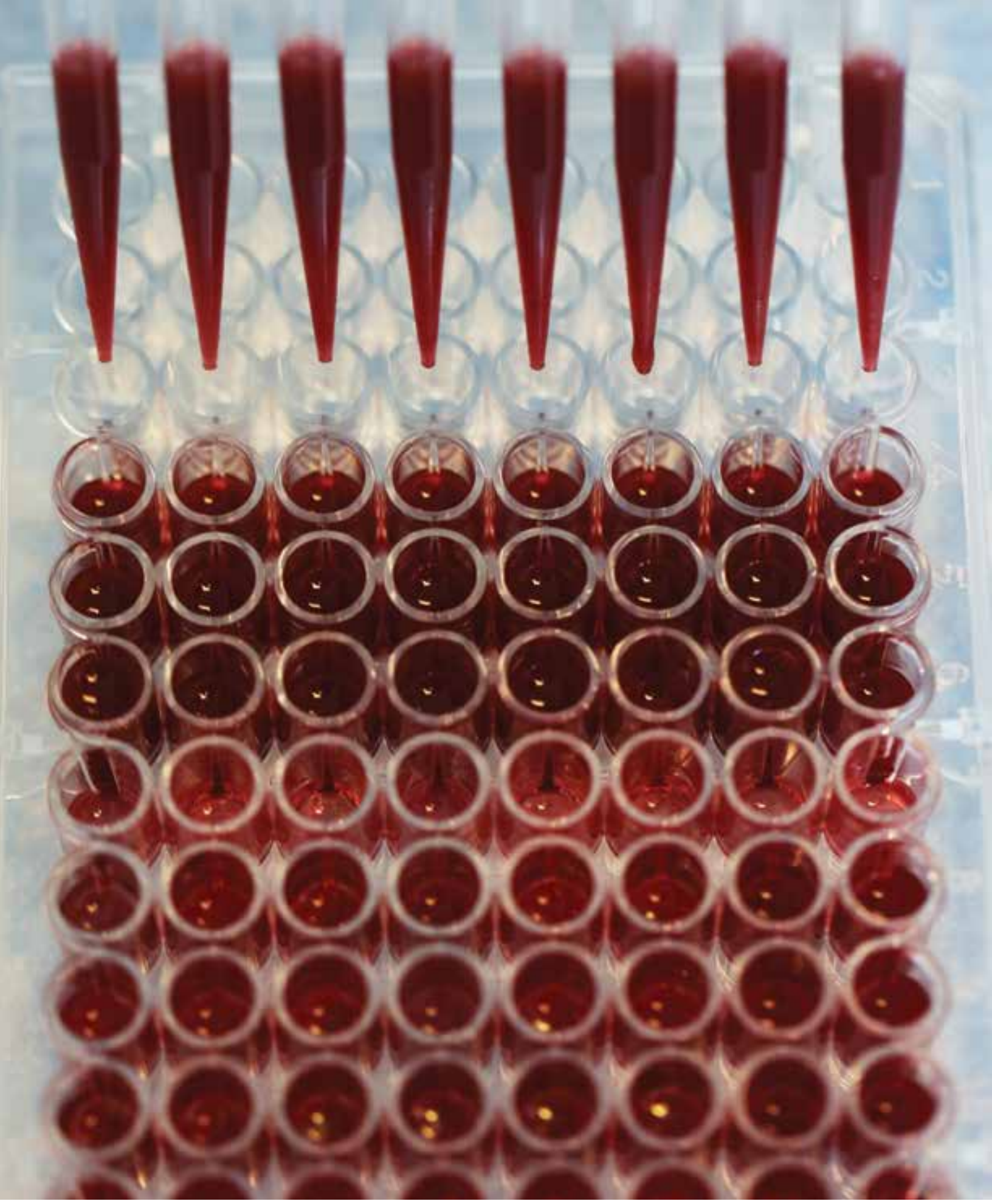
Shockingly little. Brazil has a fair amount of literature now, but most of it from the last 15 years. Argentina, where women were playing at least from the '60s, there's just one book I know of. Costa Rica, where women were playing in the '30s, there's one book. Mexico, here's not even a book, just a thesis — a bachelor's thesis.

But to get back to the question about where Latin America is vis-à-vis other countries — it varies a lot by country. Some countries have made a concerted effort in the last 20 years after ignoring or suppressing the game for quite some time. And really since the success of the women's World Cup in 1999, there's been even more of a concerted effort on the part of FIFA. FIFA gives out some money every year to every soccer federation, and a percentage of that is supposed to go to women. So that helps promote the game. But within Latin America, it's very much country by country. Chile and Colombia are working hard to develop the women's game. Colombia made it to the last World Cup and made it to the Olympics. It's an up-and-coming team and it seems like they're putting more emphasis on it. Mexico has put a lot of effort into promoting women's soccer as well.

But then you have countries like Paraguay, where the women's section is considered inactive. The women's national team doesn't play games for two or three years, and they just throw a team together when it's time for a World Cup qualifier, and of course they do very poorly. In Argentina, a number of major clubs sponsor women's amateur teams, and they'll pay for coaches, but the league is shrinking instead of growing. In Uruguay the game appears to be growing even without the support of the national federation.

But attitudes about the sport are still pretty much stuck in the 1950s or 1970s. One of the people I interviewed grew up in the U.S. and then went to play in Mexico in the '90s. She said the attitudes she faced then Mexico were the same ones she faced in the U.S. in the '70s as a soccer player.

So yes, the attitudes are somewhat behind the time. But women's youth soccer is growing in some countries. It's growing in Mexico. There's a lot of unexplored territory here. It's fascinating. Women's soccer is a lot more interesting than men's soccer for a researcher.



A Fast-Track Approach for Hypertension Treatment

Written by Marla Vacek Broadfoot / Photos by Ted Richardson

MILDRED POINTER GOES "STRAIGHT TO THE TARGET COMMUNITY" IN A CHALLENGE TO SCIENCE'S STATUS QUO

WHEN A SCIENTIST MAKES A NEW DISCOVERY, its relevance to human disease isn't always immediately apparent. It could take years of laboratory experiments and testing in animal models at the "bench," followed by clinical trials at the clinic "bedside," for researchers to know whether their findings can be translated into a new treatment or cure. The brutal truth is that this "bench to bedside" approach ends in more failures than successes, and most scientists find themselves back in the lab starting the process all over again.

Mildred Pointer, Ph.D., an associate professor in NCCU's Julius L. Chambers Biomedical/Biotechnology Research Institute (BBRI), is trying to break that cycle. She is leading an ambitious effort to take insights about hypertension gained in the laboratory directly to the communities that can benefit from them most. The project is just one example of how Pointer casts conventional wisdom aside to address problems underlying the study of human health and disease.

"I guess you can say I like to buck the system," Pointer said. "I look at the traditional paradigm and ask, 'Is this really what the data supports? Is there another perspective?' I ask those questions in everything I do, whether it is at the bench, in the community or with my students."

THE TOUGH QUESTIONS

Pointer is an amiable rebel — a lover of the scientific process who questions the status quo not to tear down others' work but to move it forward and make it more relevant. The target of her relentless inquiry is hypertension, specifically an aggressive and devastating form of the disease called salt-induced hypertension that disproportionately affects African-Americans.

People with hypertension are at increased risk for developing heart attacks, stroke or end-stage renal (kidney) disease. Hypertension is especially common among African-Americans, who are four times more likely to face an incurable renal injury than others in the general population. Conventional wisdom would suggest that treating hypertension should prevent heart attacks and renal disease, particularly in at-risk populations. But when Pointer studied the data, she found that this theory didn't hold true.

"More people are being educated about hypertension than ever before," she said. "More people are being treated for high blood pressure than ever before. We're seeing improvement in heart disease, but we're not seeing it when it comes to end stage renal disease, especially among certain sectors of the population. It's continuing to rise. So why is that? It doesn't fit. We treated the hypertension, so we should improve the end result. But it isn't working."

To investigate the problem, Pointer looked at the effects of antihypertensive agents on two different types of hypertension in rat and mouse models of the disease. While the hypertension drug completely obliterated renal injury in one form of the disease, it actually made it worse in the salt-sensitive form that is more common among African-Americans.

> "WE GET TO DEVELOP INTERVENTIONS THAT ARE SPECIFICALLY DESIGNED FOR THE CULTURE, THE ENVIRONMENT, THE PEOPLE, AND THEREFORE SAVE THE TIME AND MONEY IT TAKES TO GET FROM AN OBSERVATION IN THE LAB TO A REAL-LIFE INTERVENTION THAT WORKS IN THE COMMUNITY."
>
> —MILDRED POINTER

The finding made Pointer wonder whether the two forms of hypertension, while similar on the surface, might be caused by a very different cascade of events within the cell. Most scientists had figured that salt-sensitive hypertension was caused by an excess of sodium. Eating a lot of salt – which is made up of sodium and chloride – would cause some individuals to retain water, leading to an increased blood volume and, ultimately, a rise in blood pressure.

Yet when Pointer placed rats and mice on a high-salt diet, she found that the loss of another nutrient, calcium, rather than a rise in sodium, had the most striking impact on blood pressure. Like a key in a lock, calcium binds to specific spots along blood vessels to unlock vasodilators, the nerve chemicals that dilate the blood vessels and lead to a drop in blood pressure. Without this calcium, blood vessels are apt to constrict, causing a rise in blood pressure.

Having developed this theory in animal models, Pointer is continuing her work at the bench to explore why calcium regulation goes awry in the salt-sensitive form of the disease. "If we can understand the underlying pathophysiology, then we can develop and improve the interventions for treatment, prevention and management of salt sensitive hypertension," she said. "If we can do that, perhaps we can improve the prognosis for people with end stage renal disease."

Not wanting to limit herself to animal models and the traditional bench-to-bedside approach, Pointer tested whether the calcium quirks she uncovered in rats and mice also exist in humans with salt-sensitive hypertension. The work is part of a $5.7 million National Institute of Minority Health and Health Disparities (NIMHD) Exploratory Center of Excellence P20 grant led by Pointer and K. Sean Kimbro, Ph.D., director of BBRI. The funding contains a mixture of research and training components, focusing on diseases that disproportionately affect minorities, and also training the next generation of health disparities researchers.

"Taking a bench to curbside approach should avoid a lot of the pitfalls of traditional clinical trials because we are going straight to the target community," she said. "We get to develop interventions that are specifically designed for the culture, the environment, the people, and therefore save the time and money it takes to get from an observation in the lab to a real-life intervention that works in the community."

Pointer has linked up with investigators from nursing, public health, psychology, education, math, biology and business to set up the infrastructure needed to conduct population studies in southern Virginia and rural areas of North Carolina like Halifax County, where salt-induced hypertension is rampant. The team is conducting psychosocial surveys to assess anxiety, anger and perceived racism; banking DNA samples to look at genetic risk factors; and measuring blood chemicals such as stress hormones, lipids and insulin — all with the goal of gaining insight into the underlying causes of disease.

Her work on hypertension has found parallels between calcium levels and blood pressure in the animals housed in the laboratory and African-Americans living in the community. Further studies have also turned up genetic variants that are shared by the laboratory animals and the target population, suggesting that the results at the bench have wider implications.

"This program allows us to move from the bench to these targeted communities with ease, and back again," said Pointer. "It's a two-way street. We go in to the community to confirm our findings, but when we go there we often uncover something else. Now we can come back and fine tune our questions and make it more relevant to the real world."

BUILT TO LAST

This direct line from the laboratory to the community has benefited not only researchers and residents, but also students who are interested in biomedical research. Pointer has shepherded more than a dozen undergraduate students and as many graduate students through NCCU's P20 grant, exposing them to an environment that blends time at the bench with experience in the field.

One of her students, Sheena Nichols, has enjoyed being involved in both aspects of the lab. Her master's thesis focused on the effects of a common diuretic on interstitial calcium levels at the bench, but she also jumped at opportunities to help with population studies in North Carolina and rural Emporia, Va.

"It was exciting to see how we could link my findings together with other findings in the population," said Nichols. "I learn as I go — once I've read something I want to go out and see how it can be applied. Dr. Pointer molds you to independent learning — to be not just a doer, but a thinker."

Pointer says that giving students the opportunity to see the relevance of their research has encouraged some who had been turned off by textbooks to stick with science. In fact, all of the students who have completed the program have gone on to careers in science and related fields.

"Our goal," Pointer said, "is to continue to develop future scientists interested in doing this kind of research, scientists who are willing to become independent investigators to run their own research programs, to be at the table with some of the decision-makers, asking the leading questions for the field. That's who we want to grow."

Illustration by Tiffany DeVanzo

Through her program, Pointer has put down roots in the community that she hopes will continue to flourish even after her studies on hypertension are completed. For example, she is working with NCCU students to help with science education and tutoring in the schools and expects to see faculty members developing workshops to teach about illnesses relevant to the community. This community-academic partnership could eventually support multiple research projects, enabling investigators to ask questions about other illnesses besides hypertension, such as HIV or cancer.

"I want to see the program conducting translational research with ease and agility," she said. "I don't know of any other partnership that connects basic research from an HBCU with communities that are underserved. If we never did that, we would always be assuming the questions we're asking at the bench are relevant to the community — and that's not necessarily the case."

> "IT WAS EXCITING TO SEE HOW WE COULD LINK MY FINDINGS TOGETHER WITH OTHER FINDINGS IN THE POPULATION. I LEARN AS I GO — ONCE I'VE READ SOMETHING I WANT TO GO OUT AND SEE HOW IT CAN BE APPLIED." —SHEENA NICHOLS

TRACKING THE 'BAD PENNIES' IN SCIENTIFIC PUBLICATIONS

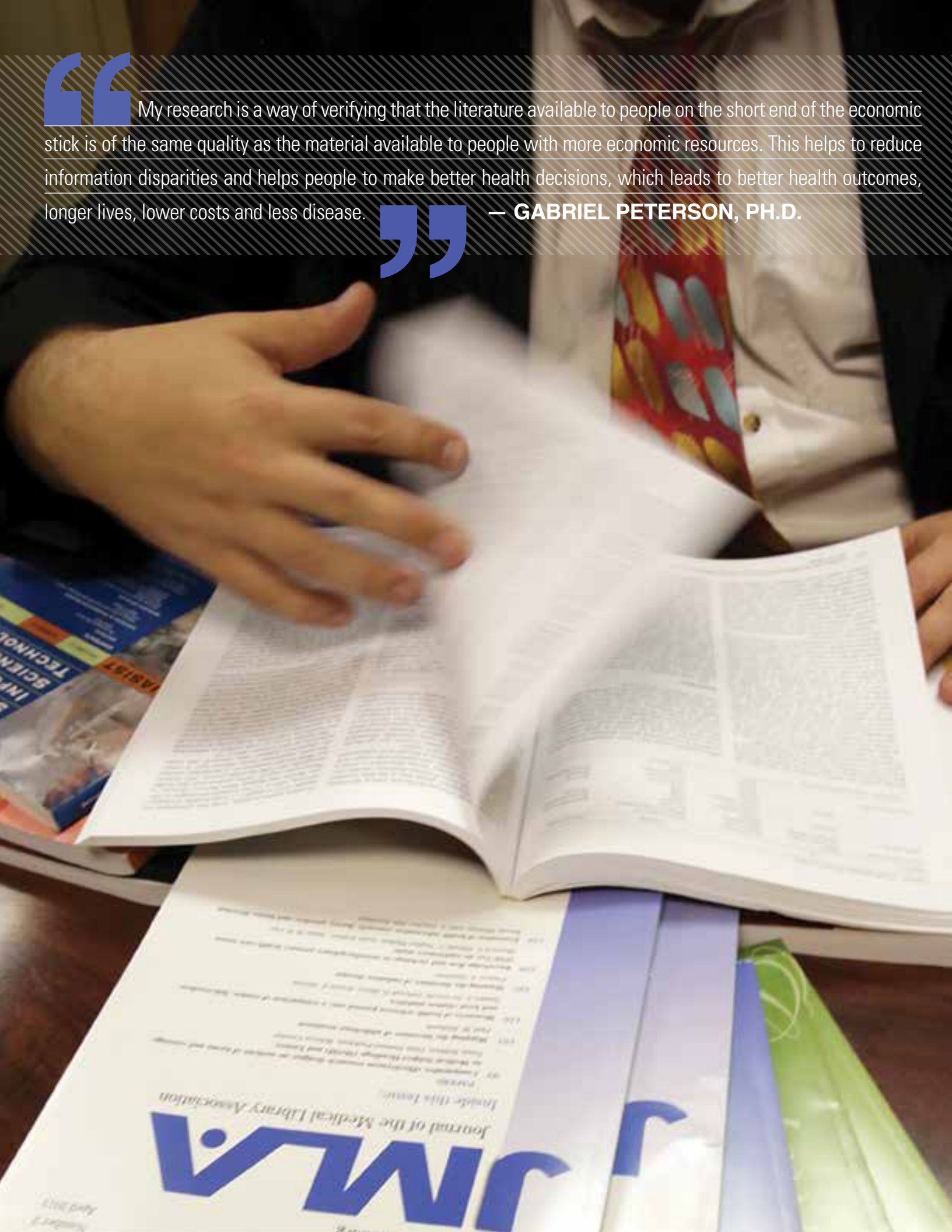
GABRIEL PETERSON SAYS SCIENCE'S 'IMMUNE SYSTEM' IS QUITE EFFECTIVE. BUT HIS RESEARCH ALSO SHOWS THAT ONCE PUBLISHED, MISINFORMATION — BOTH WILLFUL AND ACCIDENTAL — IS HARD TO CORRECT.

With the constant flow of information available online, it may seem as if the answers to any health quandary are just a click or two away. But those who aren't careful might stumble into a blog, chat room, or website inhabited by unsubstantiated claims and half-truths. Even the rare kernels of misinformation that show up in the most rigorously vetted sources — scholarly journals like Science and Nature — have a way of sticking around.

Gabriel Peterson, Ph.D., assistant professor in the School of Library and Information Sciences at North Carolina Central University, is interested in understanding how the integrity of the scientific literature is maintained and what happens when this revered resource is infiltrated by flawed or fraudulent studies.

"Because science is so open, it tends to be self-policing, making those kinds of studies rather uncommon," said Peterson. "Science is a place where you can't get away with fraud. Sooner or later someone is going to realize that what you reported doesn't make sense, or what you discovered doesn't bear up in the lab. My own research is centered on asking how well science's immune system works."

Written by Marla Vacek Broadfoot / Photos by Ted Richardson



> My research is a way of verifying that the literature available to people on the short end of the economic stick is of the same quality as the material available to people with more economic resources. This helps to reduce information disparities and helps people to make better health decisions, which leads to better health outcomes, longer lives, lower costs and less disease.
>
> **— GABRIEL PETERSON, PH.D.**

LIKE A BAD PENNY

It is an apt analogy for a researcher who once spent time at the bench conducting experiments in molecular biology and biotechnology. Peterson had already earned bachelor's degrees in biochemistry, chemistry and Spanish from New Mexico State University, as well as a master's degree in biotechnology from the University of Texas at San Antonio, when he moved to the University of Missouri to help with a research project sequencing the corn genome.

There, he ran a machine called an automated DNA sequencer, which essentially took the biological information locked within corn plants and turned it into electronic information that researchers could visualize on a computer screen.

"I came to realize that turning DNA into information was going to be the future of biology," said Peterson. "So when I sent my sequences off for analysis, I started moseying over to the computer science side of campus along with my DNA."

Eventually, Peterson stopped returning to the bench. Instead, he pursued a Ph.D. in information and library science, funded by a National Library of Medicine fellowship. During graduate school, he found his place as an intermediary — a self-described scientific linguist — between the laboratory bench scientists and the technical computer scientists. As a result, his research began to focus on the intersection between the health sciences and biomedical literature and the information society.

When Peterson came to NCCU in 2006, he continued to study the quality of scientific and health information. Despite the self-correcting nature of science, a few fraudulent studies —about 0.03 percent of the total — do make their way into the scientific literature. Once malfeasance is discovered, the offending studies are promptly retracted. But like bad pennies, a few keep showing up in the reference sections of subsequent articles. Peterson began to wonder if this problem, seen in traditional journals accessible only to scientists or elite academic institutions, might be even worse in open-access journals available to everyone.

Historically, the high publishing costs of scientific journals made them available only through subscriptions, site licenses or pay-per-view. But the spread of the Internet has made it possible to copy and distribute electronic versions of journal articles at no added cost, generating demand for open-access journals such as those published by the Public Library of Science (PLoS). Rather than passing along the cost of publishing to readers, these and other open-access journals pass along the costs to researchers, who must pay to publish their articles. Though articles can be rigorously vetted before appearing in either type of journal, some still question the quality of articles published in the open-access literature.

As part of his research, Peterson looked in the National Library of Medicine's databases and compared the number of times retracted studies were cited in fee-for-access journals like Nature or Cell versus the newer open-access journals like PLoS Medicine. He found that the levels of retraction and citation were about the same across open-access literature and fee-for-access literature, with the added bonus that disclosure was better among the open-access articles. Peterson sees the results, which were recently published in the leading journal in his field, the Journal of the American Society for Information Science and Technology, as good news. They demonstrate that this new form of literature is as reliable as the traditional literature, which many consider to be the gold standard.

"My research is a way of verifying that the literature available to people on the short end of the economic stick is of the same quality as the material available to people with more economic resources," said Peterson. "This helps to reduce information disparities and helps people to make better health decisions, which leads to better health outcomes, longer lives, lower costs and less disease."

→ Historically, the high publishing costs of scientific journals made them available only through subscriptions, site licenses or pay-per-view.

HEALTH EFFECTS

Misinformation can not only erode the public's faith in the ability of science to explain health issues, but it can also corrupt the future efforts of researchers working to test new treatments or cures for human disease. When UNC–CH researcher R. Grant Steen evaluated papers published between 2000 and 2010, he found that more than 400,000 subjects were enrolled and 70,501 patients were treated in 851 studies that cited a retracted paper.

Now Peterson is conducting a similar study, this time lowering the bar from retracted studies — those fabricated or plagiarized so that the research should be completely discounted — to flawed studies — those with errors or typos that could significantly affect how the research should be interpreted. Because those flawed studies get corrected and republished, the literature ends up with two versions of a paper that are nearly identical, except that one is reliable and the other is not.

Peterson gathered data to determine to what extent people are put at risk by the existence of these previously reported and flawed publications. So far, he has found more than 50 anomalous articles that have been cited in later research involving the treatment of human subjects.

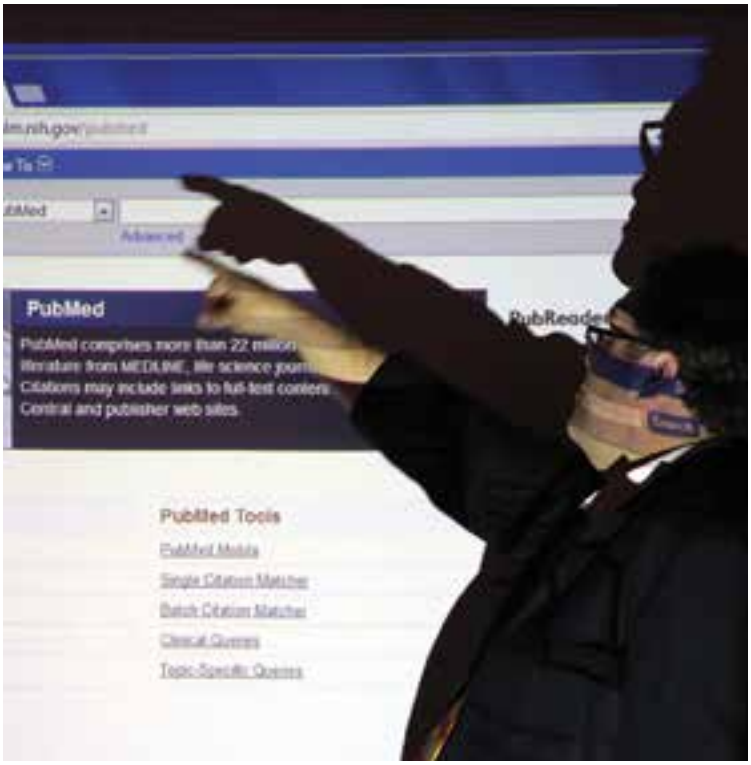
"Were they directly put at risk? Probably not, but those were human beings that were put in treatment studies that relied upon invalid scientific literature," said Peterson. "That is unacceptable."

CERTIFICATE OF AUTHENTICITY

From his own doctoral research, Peterson knows that even scholars are often unable to distinguish between flawed and scientifically valid work. Therefore, he thinks it is worthwhile to understand what factors discourage researchers from citing flawed or retracted research in order to keep these publications from reappearing in the literature.

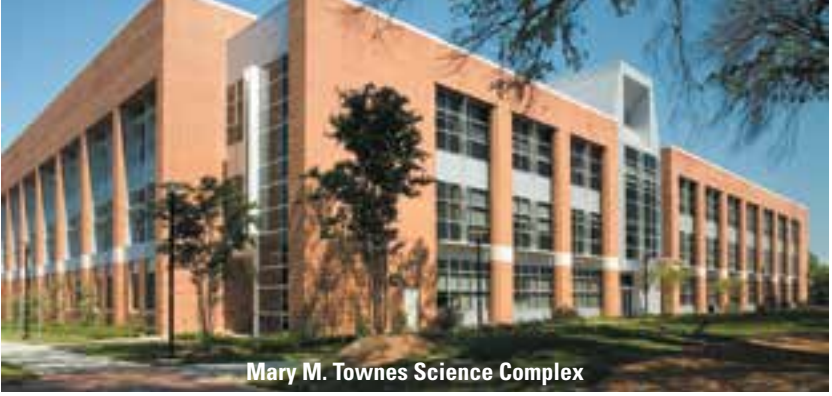
While it may seem logical to simply remove these publications altogether, Peterson says that practical and philosophical reasons make that approach untenable. Practically speaking, once papers are published online or in print, it is impossible to retrieve and discard all the errant copies. Philosophically speaking, he and others believe that even flaws and fraud should have a place in the scientific record.

"Science is a conversation that includes our mistakes, our false suppositions and our dead ends," said Peterson. "To remove errors and maleficence from the scholarly record would make the conversation less complete and less transparent, and that is not how we as scientists learn. We have to have it out there, warts and all. We have to acknowledge those mistakes and recognize them."



Still, Peterson does see some promising solutions. The current approach is to place a notation in the database entry for the flawed article. However, that puts the burden on the readers, who often overlook such corrections. Peterson thinks an approach that targets the different ways that researchers interact with literature — searching, reading, writing and publishing — would greatly curtail the propagation of error. For example, in addition to notations in databases for searchers, authors could provide a signature or other notification of authenticity to support readers. Bibliographic software to help writers spot flawed articles, and strong editorial support by publishers could help prevent authors from using flawed literature. This layered approach probably won't stop all use of flawed literature, Peterson says, but it would be an excellent start.

"Most authors want to have a way of validating their work and making sure that their word is respected by their peers," said Peterson. "Scientists generally publish with the best of intentions — their careers and their good name are on the line, so they want things to be right."



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